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US-A-3 811 840
US-A-4 088 448

JOURNAL OF MEDICAL ENGINEERING & TECHNOLOGY, vol. 5, no. 6, November 1981, pages 293-298; P. VADGAMA: "Enzyme elecrodes as practical biosensors"

(73) Proprietor: AB LEO
Box 941
S-251 09 Helsingborg (SE)

(72) Inventor: Lilja, Jan Evert
Frodes väg 17
S-291 65 Kristianstad (SE)
Inventor: Nilsson, Sven Erik Lennart
Döbeliusvägen 39
S-253 67 Helsingborg (SE)

(74) Representative: Thylén, Eva
c/o AB Leo Patent Department Box 941
S-251 09 Helsingborg (SE)

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Description

The present invention concerns a disposable cuvette for essentially simultaneous sampling a fluid and analysing of the sample.

A cuvette for sampling a fluid, mixing the sample with a reagent and directly making optical analyses of the sample mixed with the reagent is previously known from the US patent 4,088,448. This cuvette comprises a body member including two planar surfaces defining an optical path and placed at a predetermined distance from one another to determine the optical path length and to define a cavity having an inlet communicating said cavity with the exterior of the body member.

The cavity has a predetermined fixed volume, and the predetermined distance permits the sample to enter the cavity by capillary force. Furthermore, a reagent is coated on the cavity surface.

This known cuvette has several advantages when compared with the conventionally used devices. It permits sampling of a liquid, mixing and chemically reacting it with a suitable reagent for e.g. colour development in the same vessel as the one used for the subsequent measurement. The cuvette disclosed in the US patent 4,088,448 thus simplifies the sampling procedure, reduces the number of utensiles and in most cases, depending on the type of analysis considerably improves the exactitude of the analysis by making the analysing procedure independent of the operating technique of the operator making the analysis.

The present invention concerns an improvement of this known cuvette.

To this end there has been developed a disposable cuvette for essentially simultaneous sampling a fluid and analysing the sample comprising a body member having at least one cavity defined by surrounding walls, into which cavity a sample is permitted to enter by capillary force through an inlet communicating said cavity with the exterior of said body member, characterized in that at least one part of the walls facing the cavity consists of a simipermeable membrane.

One advantage with this improved cuvette is that it can be used for other types of measurements than optical analyses, which makes it applicable for analyses within a much broader range than the cuvette according to the US patent 4,088,448. Thus, according to the present invention, the measurement can be carried out by using different electrodes, the surfaces of which are pressed against the exterior surface of the semipermeable membranes, in addition to the use of optical instruments. Within the scope of the present invention are also electrode or sensor systems integrated with, i.e. applied on or incorporated in, the semipermeable membrane material.

Another very important advantage as compared with the previously known cuvette is that the use of membranes gives a possibility to separate sample media from reagent media and interferences originating from substances, unsuitable pH, unsuitable redox environment etc. can be avoided. Thus, two or more reaction systems, which are incompatible, can be included in the new cuvette, as the semipermeable membrane acts as a barrier, which prevents a component, e.g. a reagent contained in the cavity from entering and disturbing the reaction(s) in the membrane(s) and vice versa. This second advantage makes the field of application for the present cuvette even broader and applicable to a wide variety of different analyses.

Thus, the additional advantages according to the present invention emanate from the use of the semipermeable membrane and the possibility to combine this membrane with external or internal electrodes.

Analyses based on the use of semipermeable membranes and electrodes are known in the art. According to the known technique, however, there are problems with the handling of the sample, contamination of the electrodes, which often are sensitive to contamination, evaporation of the sample and the influence of different types of gases, such as air oxygen. All these problems can be avoided by using the cuvette according to the present invention.

According to the present invention the body member may consist of glass or polymeric material. It is also quite possible to make the whole body member or one wall thereof of the semipermeable material, which in this case preferably should be self-supporting. If not essentially self-supporting, the membrane could be used as a coating on the surface of the body member facing the cavity. The reagent, if any, coated on at least a part of the (body member) surface facing the cavity may be deposited by evaporation, freeze-drying, spraying or screen-printing as known in the art.

The semipermeable membrane may be in the form of one separate membrane layer or two or more separate layers joined to each other to form a composite membrane. The various reagents may be coated on the membrane surface facing the cavity and applied thereon by evaporation, freeze-drying, spraying or screen-printing, etc. It is also possible to have the reagents deposited as a layer on the separate surfaces of the membrane in such a way that this layer becomes an intermediate layer in the finished composite membrane. One or more such layers may be present. The semipermeable membrane may also be prepared in such a manner that the reagent or reagents are dispersed or dissolved throughout the whole membrane or one or more layers thereof. Another possibility is to prepare the membrane material in such a manner that the reagent molecules are covalently bound to the polymers of the semipermeable membrane.

The semipermeable membrane material is chosen depending on the kind of analysis to be performed and it could be determined by a person skilled in the art. The membrane material might be hydrophilic or hydrophobic. Examples

of different material, which can be used according to the present invention are Teflon®, silicon rubber, polyacrylates, polyvinyles, collagen and even crosslinked enzymes, etc. Various substances could be incorporated in the membrane to give special selective properties, to perform a chemical reaction, etc. Including specific crown ethers in a polyvinyl membrane gives a membrane with selective properties for alkaline ions. Including glucose oxidase in a membrane makes it possible to measure glucose by the production of hydrogen peroxide or the decrease in oxygen concentration.

The membrane may selectively permit penetration of only or essentially the substance/ion, which is relevant/interesting, and which can be detected by for example an electrode on the external surface of the membrane. Furthermore, the membrane may function as a discriminator in which only molecules/ions below a certain size can move freely.

To perform measurements with electrodes on or in the improved cuvette, the membrane acts as a semi-permeable barrier (with or without selective properties) which prevents the electrode from being contaminated by the sample media and/or the reagents. The membrane could participate in a chemical reaction through incorporated reagents and/or selectively permit free passage way for the species to be determined at the electrode.

The electrode to be used according to the present invention might be a conventional potentiometric, i.e. ion-selective or amperometric electrode, which together with the semipermeable membrane of the cuvette, functions as an enzyme electrode or biosensor of the kind described in e.g. P Vadgama, Journal of Medical Engineering & Technology, Vol 5, No. 6, 1981, 293-298.

Examples of electrodes to be used with the membrane cuvette of the present invention are conventional electrodes, such as the glass electrode (pH), the platinum, gold, or carbon electrode and other, more exclusive electrodes, such as solid state devices such as CHEMFET's or ISFET's with its associated electronic parts.

An example of a platinum/silver-silver chloride electrode system together with a composite membrane for determining glucose by amperometric measurement of consumed oxygen is given in an article by Jean-Louis Romtte, B Fromment & D Thomas, (Clin.-Chim.Acta, 95 (1979) 249-253).

An example of glass electrode application together with a composite membrane for determining urea by pH-measurement of produced ammonia is disclosed in an article by M Mascini and G G Guilbault, (Anal.Chem., Vol. 49, No. 6, May '77, 795-798).

As regards optical analyses to be performed with the present cuvette, there are two main possibilities:

A The colour develops in the cavity

B The colour develops within the membrane

In "A" the two main surfaces of the cavity must have a predetermined or a determinable distance between one another to make it possible to determine the optical path length. The determinable distance could be obtained by applying external force on the surface of an essentially elastic membrane until the movement of the membrane is stopped against a spacer of predetermined thickness inserted in the cavity.

In "B" the colour developing part (layer) of the membrane or the entire membrane must be of a predetermined thickness to accomplish a determined optical path length.

A practical example of "B" is a cuvette designed to perform an analysis of urea in serum or urine. The cavity contains urease and an alkaline buffer system in dry form which when dissolved in the sample media give free ammonia from urea, and the membrane incorporates an indicator (= a reagent) for ammonia. The membrane is manufactured from a polymer the hydrophobicity of which is sufficiently high to prevent interference from the alkaline buffer onto the indicator, but permeable to ammonia. The indicator is a solvent soluble pH-indicator with an indicator range within the acid area.

Different approaches to the analyses could be made by using different types of electrodes, different types of membranes and different reaction routes as recognized by a person skilled in the art.

The invention will be described more in detail in the following with reference to the accompanying drawings, which schematically and on a large scale illustrate several embodiments. In the drawings:

FIG 1 shows a measuring cuvette according to the invention.

FIG 1a shows a section on the line I-I in FIG I.

FIG 2a shows a modified embodiment of the cuvette.

FIG 2b shows a view of FIG 2a.

FIG 3 shows the cuvette according to FIG 2 and 2a in contact with a measuring electrode.

FIG 4 shows the cuvette according to FIG 2 and 2a adapted for optical measurement.

FIG 5 shows an embodiment in which the cuvette has parallel-connected cavities.

FIG 5a shows a section on the line II-II.

FIG 6 shows a further modified embodiment of the cuvette.

FIG 6a shows a section on the line III-III.

The cuvette illustrated in FIG 1 and 1a comprises a body wall 10 of glass or polymeric material, and a body wall 11 of semipermeable membrane material. The walls define a cavity 12 which is intended to accomodate a liquid sample and the dimension of which is such that it can be filled by capillary force. Two channels 13 which extend from opposite sides of the cuvette and open into the cavity 12. Thus a sample can here be drawn straight through the cuvette, which may be advantageous in certain cases. The cavity 12 might be supplied with a reagent (that is an agent to react with the sample drawn into said cavity) by evaporation, freeze-drying, spraying, screen-

printing or in another suitable manner according to the manner in which the cuvette is manufactured.

The wall 11 of semipermeable membrane material might be manufactured in such a manner that a reagent system is incorporated in the membrane, e.g. dispersed or dissolved in the membrane. It is also possible to manufacture the membrane in such a way that the components (molecules) of the reagent system are covalently bound to the polymers constituting the membrane material. Another possibility is to build up a semipermeable membrane of two or more layers and apply the reagent system or systems as intermediate layers between two adjacent membrane layers. One or more such layers and intermediate layers may be present. All types of combinations of incorporation of the reagent system apparent to the skilled in the art fall within the scope of the present invention.

In FIG 2a 10 is body wall of polymeric supporting material. 11 is a semipermeable membrane optionally composed by several layers. 12 is the cavity accomodating the sample. Elevations 14 determine the optical path length. When the sample is drawn into the cavity 12, air is pressed out through the slit 15. The body wall 10 and the semipermeable membrane 11 are brought together along the joint 16 (a weld joint or a glue line). The area 17 indicates a suitable measuring zone.

In FIG 3 a measuring electrode is brought into contact with the semipermeable membrane 11 in the cuvette disclosed in FIGs 2a and 2b. In this special embodiment the electrode consists of a platinum electrode 18 and a reference silver/silver chloride electrode 19. 20 designates the glass body surrounding the platinum electrode 18.

In FIG 4 the cuvette of the FIGs 2a and 2b is adapted for optical measuring. Thus here 21 designates a light source for e.g. monochromatic light. 22 indicates the light way towards the cuvette. 23 indicates the light way for not absorbed light after the cuvette, and 24 is an optical detector.

The cuvette as shown in FIG 5 has four parallel-connected cavities 25, 25' which are linked to a common channel 26 by branch channels 27 which continue on the opposite side of the cavities and open into the atmosphere to prevent air inclusions in the cavities, when samples are drawn thereinto. Different reactive systems might be included in the different cavities and/or the membrane material defining the whole or part of the cavity.

FIG 5a shows a section of the cuvette according to FIG 5 along the line II-II.

The embodiment of the present invention according to FIG 6 and 6a consists of elastic semipermeable material. The inlet channel 28 is communicating the exterior of the cuvette with the cavity 12.

While the invention has been described with reference to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made without departing from the invention as claimed by the claims. Many alternative container designs can be conceived which will achieve the advantageous results herein disclosed.

Further, it is contemplated that any analytical procedure can be adapted to the herein disclosed invention. The cuvette herein disclosed is particularly suitable for routine blood chemistry, such as glucose, blood urea nitrogen, albumin, bilirubin, total protein, etc., and numerous other analytical tests.

Accordingly, all substitutions, additions, and modifications to which the present invention is readily susceptible, without departing from the invention as claimed by the claims.

Claims

1. Disposable cuvette for essentially simultaneous sampling a fluid and analysing the sample comprising a body member having at least one cavity (12, 25, 25') defined by surrounding walls (10, 11), into which cavity (12, 25, 25') a sample is permitted to enter by capillary force through an inlet (13, 26, 27, 28) communicating said cavity (12, 25, 25') with the exterior of the body member characterized in that at least one part of the walls (10, 11) facing the cavity (12, 25, 25') consists of a semipermeable membrane.

2. Cuvette according to claim 1 characterized in that an electrode and/or sensor system is integrated with the semipermeable material.

3. Cuvette according to claim 1 or 2 characterized in that at least one reagent or reagent system is incorporated in the cuvette.

4. Cuvette according to any of the preceding claims characterized in that the semipermeable membrane consists of one or more layers.

5. Cuvette according to any of the preceding claims characterized in that at least one reagent or reagent system is incorporated in or coated on the semipermeable membrane or one or more layers thereof.

6. Cuvette according to any of the preceding claims characterized in that a reagent or reagent system is dispersed or dissolved in the membrane or at least one layer thereof and/or applied as at least one intermediate layer between two adjacent membrane layers.

7. Cuvette according to any of the preceding claims characterized in that molecules of the reagent or reagent system are covalently bound to the polymers of the semipermeable membrane or a layer thereof.

8. Cuvette according to any of the preceding claims characterized in that a reagent or reagent system is coated on at least a part of the surface facing the cavity.

9. Cuvette according to any of the preceding claims characterized in that two planar surfaces of the cavity define an optical path length.

10. Cuvette according to any of the preceding claims characterized in that the semipermeable membrane or a layer thereof has a predetermined fixed thickness defining an optical path length.

Patentansprüche

1. Einwegküvette zur Entnahme einer Flüssigkeitprobe im wesentlichen gleichzeitig mit der Analyse der Probe, umfassend einen Körper mit zumindest einem Hohlraum (12, 25, 25'), welcher von umgebenden Wänden (10, 11) abgegrenzt ist und in welchen eine Probe durch einen den Hohlraum (12, 25, 25') mit der Aussenseite des Körpers verbindenden Einlauf (13, 26, 27, 28) durch Kapillarkraft eintritt, dadurch gekennzeichnet, dass zumindest ein Teil der dem Hohlraum (12, 25, 25') zugewandten Wände (10, 11) aus einer halbdurchlässigen Membran besteht.

2. Küvette nach Anspruch 1, dadurch gekennzeichnet, dass eine Elektrode und/oder ein Sensorsystem mit dem halbdurchlässigen Material integriert ist.

3. Küvette nach Anspruch 1 oder 2, dadurch gekennzeichnet, dass der Küvette zumindest ein Reagens oder Reagenssystem einverleibt ist.

4. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die halbdurchlässige Membran aus einer oder mehreren Schichten besteht.

5. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass der halbdurchlässigen Membran oder einer oder mehreren Schichten davon zumidest ein Reagens oder Reagenssystem einverleibt oder aufgetragen ist.

6. Küvette nach einem der vohergehenden Ansprüche, dadurch gekennzeichnet, dass in der Membran oder zumindest einer Schicht davon ein Reagens oder Reagenssystem dispergiert oder aufgelöst und/oder als zumindest eine Zwischenschicht zwischen zwei benachbarten Membranschichten angebracht ist.

7. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass Moleküle des Reagenses oder Reagenssystems mit den Polymeren der halbdurchlässigen Membran oder einer' Schicht davon kovalent gebunden sind.

8. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass zumindest einem Teil der dem Hohlraum zugewandten Fläche ein Reagens oder Reagenssystem aufgetragen ist.

9. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass zwei ebene Flächen des Hohlraums einen Lichtweg abgrenzen.

10. Küvette nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, dass die halbdurchlässige Membran oder eine Schicht davon eine vorbestimmte, festgelegte Dicke hat, welche einen Lichtweg abgrenzt.

Revendications

1. Cuvette jetable permettant de procéder, pour l'essentiel simultanément, à l'échantillonnage d'un fluide et à une analyse de l'échantillon, présentant un corps muni d'au moins une cavité (12, 25, 25') délimitée par des parois environnantes (10, 11), cavité dans laquelle une éprouvette peut pénétrer par capillarité, par l'intermédiaire d'un orifice d'admission (13, 26, 27, 28) faisant communiquer ladite cavité (12, 25, 25') avec l'extérieur dudit corps, caractérisée par, le fait qu'au moins une partie des parois (10, 11) faisant face à la cavité (12, 25, 25') consiste en une membrane semiperméable.

2. Cuvette selon la revendication 1, caractérisée par le fait qu'un système à électrodes et/ou à détecteur est intégré au matériau semi-perméable.

3. Cuvette selon la revendication 1 ou 2, caractérisée par le fait qu'au moins un agent réactif ou système réactif est incorporé dans cette cuvette.

4. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait que la membrane semiperméable comprend une ou plusieurs couches.

5. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait qu'au moins un agent, réactif ou système réactif est incorporé dans da membrane semi-perméable ou déposé sur cette dernière, ou bien l'une ou plusieurs de ses couches.

6. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait qu'un agent réactif ou système réactif est dispersé ou dissous dans la membrane ou au moins l'une des couches de celle-ci, et/ou appliqué entre deux couches adjacentes de la membrane, sous la forme d'au moins une couche intercalaire.

7. Cuvette selon l'une quel'conque des revendications précédentes, caractérisée par le fait qu'une liaison covalente est établie entre des molécules de l'agent réactif ou du système réactif, et les polymères de la membrane semi perméable ou d'une couche de cette dernière.

8. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait qu'un agent réactif ou système réactif est déposé sur au moins une partie de la surface tournée vers la cavité.

9. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait que deux surfaces planes de la cavité définissent une longueur de trajet optique.

10. Cuvette selon l'une quelconque des revendications précédentes, caractérisée par le fait que la membrane semiperméable ou une couche de celle-ci présente une épaisseur fixe prédéterminée, définissant une longueur de trajet optique.

FIG. 1

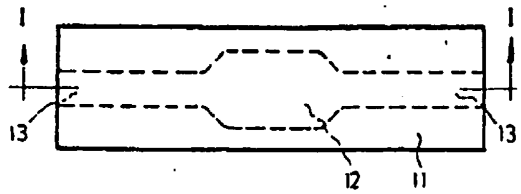

FIG. 1a

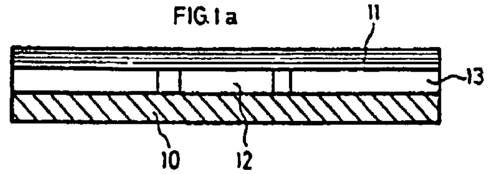

FIG. 2a

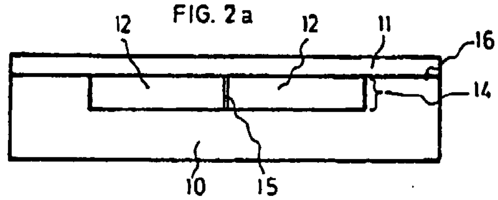

FIG. 2b

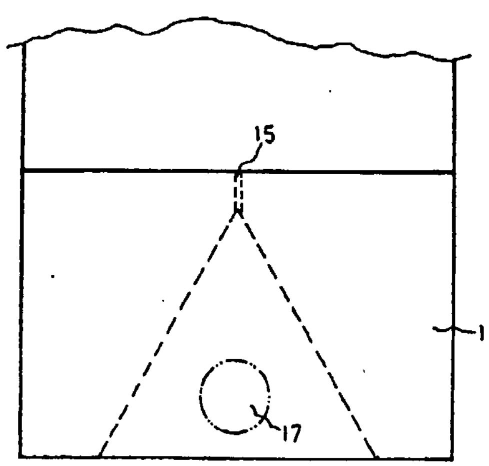

FIG. 3

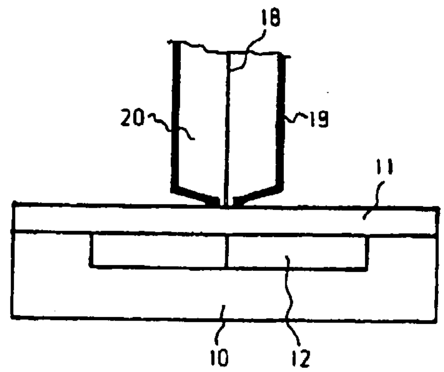

FIG. 4

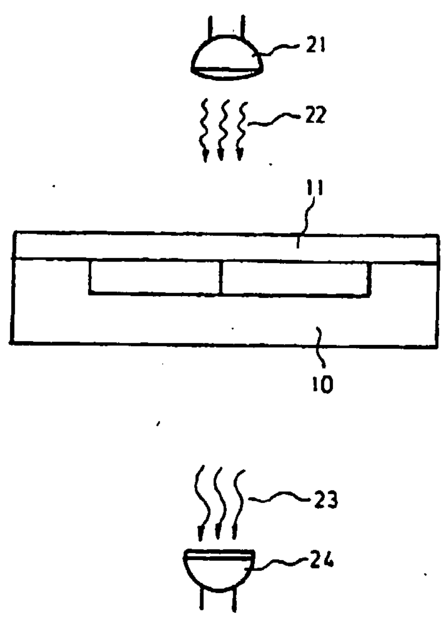

FIG. 5

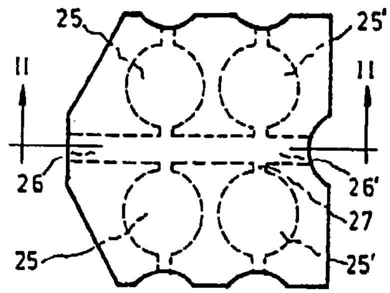

FIG. 5a

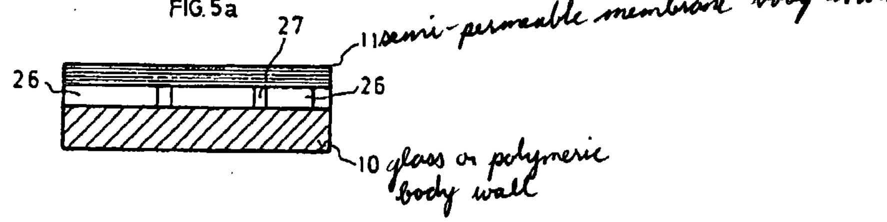

FIG. 6

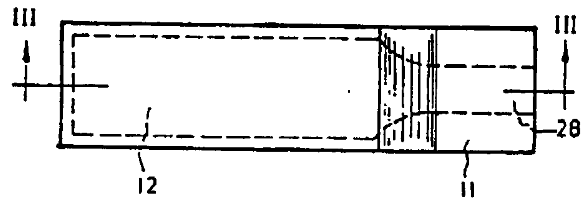

FIG. 6a